UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,417	01/16/2004	Beth A. Burnside	PHARMA-0142-C02	5644

24999 7590 11/29/2007

MILLEN, WHITE, ZELANO & BRANIGAN, PC
2200 CLARENDON BLVD
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
CARTER, KENDRA D	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,417	BURNSIDE ET AL.	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 19-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 19-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of September 18, 2007 made to the office action filed April 18, 2007. Claims 1-7 and 19-56 are pending. Claim 34 is amended and claim 57 is cancelled.

The Examiner has acknowledged that the Mulye reference (US 6,475,493 B1) has priority of September 2, 1999 and therefore does not qualify as prior art because of the Applicant's priority to application 09/176,542, now patent US 6,322,819, was filed October 21, 1998. Therefore, all prior rejections are withdrawn.

Due to the above withdrawal of all rejections, a new non-final office action is below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(1) Claims 1-17 and 19-57 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 and 21-24 of U.S. Patent No. 6,322,819 B1 ('819) in view of Berger (US 3,344,029), in view of Millman (US 2,881,113), in further view of Meyer (US 5,322,697).

Although the conflicting claims are not identical, they are not patentably distinct from each other.

The patent '819 teaches a pharmaceutical composition for delivery of one or more pharmaceutically active amphetamine salts comprising: (a) one or more amphetamine salts covered with an immediate release coating; and (b) one or more amphetamine salts covered with an enteric release coating that provides for delayed pulsed enteric release (see claims 1, 8, 13 and 18). The enteric release coating has a thickness of at least 25μ (see claim 2). The amphetamine salts can be coated onto a core or incorporation into a core (see claims 3, 4, 9, 10, 14, 15, 21 and 22). The amphetamine salts can be coated with an immediate release coating and an enteric

release coating on a single core or on different cores (see claims 5, 11, 12, 16, 17, 23 and 24). The enteric release coating can be a non-pH dependent (see claim 7). A composition further comprises a protective layer over the enteric release coating or a protective layer between the amphetamine salt and the enteric release coating (see claims 13 and 18).

The patent '819 does not teach the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate, or the dosage amounts. A pharmaceutically acceptable carrier, an anionic copolymer based on methacrylic acid and acrylic acid ethyl ester, properties, dosage amounts, or method of treatment of the composition as disclosed in claims 19, 20, 28-32, 36-39, 42, 43, 46-53 are not taught. The patent '819 also does not teach a second layer surrounding the first layer and the first layer surrounding the core, or wherein the amphetamine salts are provided in about the same amounts.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35

and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22). The amphetamine compounds are added in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3).

Meyer teaches a composition administered in a tablet form that controls appetite. The composition is formulated so that the active ingredient is release predominately in the ileum (see abstract). The preferred enteric coating is a pH sensitive polymer that dissolves at the neutral to slightly alkaline pH of the human ileum (pH 7.5). A commonly used currently approved coating of this nature is Eudragit S (see column 9, lines 37-41). Amphetamine is a common appetite suppressant drug (see column 1, lines 16-17).

In regards to the method of treatment of the composition, these factors are not considered in composition claims. The claims are only treated on the merits as related to a composition. Also, in regards to the properties of the composition, including the pulsed enteric coating, they are inherent to the composition because where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established. Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ

430, 433 (CCPA 1977). The above applies to claims 1, 6, 10, 15, 17, 20, 28-30, 36-39, 42, 43, 46-51 and 53 and to all further rejections of these claims.

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '819 and the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate or wherein the amphetamine salts are provided in about the same amounts, and its dosage amount because they are species of the genus amphetamine salts. Without unexpected results, the above amphetamine salts should perform the same as the genus. Additionally, Berger teaches a controlled release composition comprising dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18. In regards to the amounts, Berger teaches that the therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10). Additionally, Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22), in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3). It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine '819 and an anionic copolymer based on methacrylic acid and acrylic acid ethyl ester, and soluble at a pH of about 5.5 upwards (applicant's claim 53) because of the following teachings: 1) Berger teaches a composition comprising amphetamines with an enteric coating; 2) Meyer teaches a tablet that controls appetite comprising a pH sensitive polymer that dissolves at the neutral to slightly alkaline pH of the human ileum (pH 7.5), in which Eudragit S is commonly used (see column 9, lines 37-41); and 3) Meyer also teaches that the composition is formulated so that the active ingredient is released predominately in the ileum (see abstract), and Amphetamine is a common appetite suppressant drug (see column 1, lines 16-17). Thus, one would be motivated to provide better release profiles of amphetamines by incorporating the specific enteric coating agent disclosed in Applicant's claim 53.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine '819 and a second layer surrounding the first layer and the first layer surrounding the core because Berger teaches that control of the active agent within the body is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings. Thus, it is within the

art to adjust the tablet coatings to achieve the desired effects of release in the human body.

(2) Claims 1-4, 6-13, 15-17, 19-24, 26, 28-32, 34-44, 46-54, 56 and 57 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 10-14 of U.S. Patent No. 6,605,300 B1 ('300) in view of Berger (US 3,344,029), in view of Millman (US 2,881,113), and in further view of Nash et al. (US 2,993,836).

Although the conflicting claims are not identical, they are not patentably distinct from each other.

The patent '300 teaches a pharmaceutical formulation for delivery of a mixture of amphetamine base salts effective to treat ADHD comprising an immediate release dosage form; a delayed enteric release dosage that provides delayed release upon oral administration; and a pharmaceutically acceptable carrier; wherein said amphetamine base salts comprise dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate containing about a total dose of 20 mg (see claims 1 and 12). The enteric release dosage form comprises a coating of a thickness of at least 20 μm or 25 μm (see claims 10, 11 and 13). The formulation further comprises an anionic copolymer (see claim 14).

The formulation of '300 does not teach the properties of the composition, a delayed release that is pH independent, or a protective layer. Also, the amphetamine salts coated onto a core or incorporated into a core, or wherein the immediate release and enteric release portions are present on a single core is not taught. Lastly, the amphetamine salts provided in about equal amounts is not taught.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see

column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22). The amphetamine compounds are added in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3).

Nash et al. teaches an improvement in pharmaceutical sustained release tablets, in which a sustained release tablet breaks down uniformly in an aqueous medium independent of pH and/or the presence of enzymes (see column 1, lines 10-16). Thus,

when administered to a patient, the uniform release absorption at a uniform rate regardless of the part of the gastrointestinal tract in which the tablet lies (see column 1, lines 33-36). Therapeutic agents that are used in the tables are dextro-amphetamine sulfate (see column 2, line 67).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '300 and a delayed release that is pH independent, a protective layer, wherein the amphetamine salts coated onto a core or incorporated into a core, or wherein the immediate release and enteric release portions are present because of the following teachings: 1) Berger teaches that control of the active agent within the body is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings; 2) Berger also teaches a pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24); 3) Berger teaches that the therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10); 4) Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22), in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3); 4) it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.); and 5) Nash teaches an improvement in pharmaceutical sustained release tablets, such as amphetamines, in which a sustained release tablet breaks down uniformly in an aqueous medium independent of pH and/or the presence of enzymes (see column 1, lines 10-16).

The patent '300, Berger, and Nash references are all controlled release compositions. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

(3) Claims 1-5 and 15-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9, 11, 12, 14-17, 19, 21, 23, 24, 29 and 35-37 of U.S. Patent No. 6,913,768 B2 ('768) in view of Berger (US 3,344,029).

Although the conflicting claims are not identical, they are not patentably distinct from each other.

The patent '768 teaches a pharmaceutical composition comprising a mixture of amphetamine salts and a sustained release coating or matrix for a 20 mg total dose (see claims 1, 7, 11, 12, 14, 15, 24, 31, and 35). The composition specifically comprises a mixture of dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate and also in equal amounts by weight (see claims 2, 3, 19, and 36). The amphetamine salts are provided in a core which is coated with a dissolution regulating agent that provides sustained release (see claims 4, 5, 17, 21, 23, 24, and 29). The sustained release coating or matrix has a pH independent dissolution release (see claim 31).

The patent '768 does not teach the properties of the composition, an immediate release coating, or an enteric release coating with a thickness of at least 25μ.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines

47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '768 and an immediate release coating and an enteric release

coating with a thickness of at least 25μ because Berger teaches that further control of dissolution is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Thus, the thickness of the enteric coated pellet can be adjusted by one skilled in the art to achieve the desired dissolution properties. It is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of the result effective variable in a known process is ordinarily within the skill of the art." See, e.g., In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Paterson* Appeal No. 02-1189 (Fed. Cir. January 8, 2003).

The patent '768 and Berger compositions are controlled release compositions. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

(4) Claims 1-4, 6-13, 15-17, 19-26, 28-44, 46-54, 56 and 57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 11/091,010 ('010) in view of Berger (US 3,344,029).

This is a provisional obviousness-type double patenting rejection.

The application '010 teaches a pharmaceutical formulation for delivery of a mixture of amphetamine base salts effective to treat ADHD comprising an immediate release dosage form; a delayed enteric release dosage that provides delayed release upon oral administration; and a pharmaceutically acceptable carrier; wherein said amphetamine base salts comprise dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate containing about a total dose of 20 mg (see claim 1). The enteric release dosage form comprises a coating of a thickness of at least 20 μm or 25 μm (see claims 10-13) and the salts are contained in about equal amounts within each of said dosage forms (see claim 9). The formulation further comprises an anionic copolymer (see claims 10, 12 and 14). The coating is soluble at a pH of about 5.5 upwards (see claims 10 and 12). The formulation maintains an effective level of amphetamine salts in the patient over the course of at least 8 hours without further administration and the peak plasma concentration reached

after release of said delayed enteric release dosage form exceeds the peak plasma concentration previously reached after release of said immediate release dosage form (see claim 1). The dosage amounts are 20 mg to produce a plasma concentration versus time curve having an area under the curve (AUC) of about 467 to about 714 ng hr/ml, and a maximum concentration (C_{max}) of about 22.5 to about 40 ng/ml for about 7 to about 10 hours (see claims 1-8 and 15-17). The composition is formulated such that the total amphetamine dose having an AUC proportional to the AUC of a composition formulated for a 20 mg total amphetamine dose, and having a C_{max} proportional to the C_{max} for a 20 mg total amphetamine dose (see claims 17 and 18). The delayed release is pH independent and the composition further comprises a protective coating layer (see claims 19 and 20).

The application '010 does not teach the amphetamine salts coated onto a core or incorporated into a core, or wherein the immediate release and enteric release portions are present on a single core.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35

and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '010 and wherein the amphetamine salts coated onto a core or incorporated into a core, or wherein the immediate release and enteric release portions are present because Berger teaches the following: 1) a tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract; 2) the cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51); and 3) further control of dissolution is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6).

The application '010 and Berger compositions are controlled release compositions. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re*

Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

(5) Claims 1-17 and 19-57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8-18 21-24 and 26 of copending Application No. 11/091,011 ('011) in view of Berger (US 3,344,029), in view of Millman (US 2,881,113), in further view of Meyer (US 5,322,697).

This is a provisional obviousness-type double patenting rejection.

The application '011 teaches a pharmaceutical formulation for delivery of a mixture of amphetamine base salts comprising an immediate release dosage form; and a delayed enteric release dosage that provides delayed release upon oral administration wherein the enteric release dosage form comprises a coating of a thickness of at least 25 μm (see claims 1, 2, 5, 8, 11, 13, and 18). The amphetamine salts are coated onto a core or incorporated into a core (see claims 3, 4, 14, and 15) The amphetamine salts are covered with an enteric release coating on a single core or covered with an immediate release coating on one core and amphetamine salt covered with an enteric release coating on a different core (see claims 5, 6, 11, 12, 16, 17, 21, 22, 23 and 24). The delayed pulse enteric release of amphetamine salt increases the

blood level of amphetamine salt to a second level that is greater than the first level provided by the component (see claims 8 and 11). The formulation further comprises a protective layer over the enteric release coating (see claim 13).

The application '011 does not teach the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate and its dosage amount. A pharmaceutically acceptable carrier, an anionic copolymer based on methacrylic acid and acrylic acid ethyl ester, properties, dosage amounts, or method of treatment of the composition as disclosed in claims 19, 20, 28-32, 36-39, 42, 43, 46-53 are not taught. The application '010 also does not teach a second layer surrounding the first layer and the first layer surrounding the core, or wherein the amphetamine salts are provided in about the same amounts.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of

therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22). The amphetamine compounds are added in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3).

Meyer teaches a composition administered in a tablet form that controls appetite. The composition is formulated so that the active ingredient is release predominately in the ileum (see abstract). The preferred enteric coating is a pH sensitive polymer that dissolves at the neutral to slightly alkaline pH of the human ileum (pH 7.5). A commonly used currently approved coating of this nature is Eudragit S (see column 9, lines 37-41). Amphetamine is a common appetite suppressant drug (see column 1, lines 16-17).

In regards to the method of treatment of the composition, these factors are not considered in composition claims. The claims are only treated on the merits as related to a composition. Also, in regards to the properties of the composition, including the pulsed enteric coating, they are inherent to the composition because where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established. Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ

430, 433 (CCPA 1977). The above applies to claims 1, 6, 10, 15, 17, 20, 28-30, 36-39, 42, 43, 46-51 and 53.

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '011 and the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate or wherein the amphetamine salts are provided in about the same amounts, and its dosage amount because they are species of the genus amphetamine salts. Without unexpected results, the above amphetamine salts should perform the same as the genus. Additionally, Berger teaches a controlled release composition comprising dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18. In regards to the amounts, Berger teaches that the therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10). Additionally, Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22), in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3). It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine '011 and an anionic copolymer based on methacrylic acid and acrylic acid ethyl ester, and soluble at a pH of about 5.5 upwards (applicant's claim 53) because of the following teachings: 1) Berger teaches a composition comprising amphetamines with an enteric coating; 2) Meyer teaches a tablet that controls appetite comprising a pH sensitive polymer that dissolves at the neutral to slightly alkaline pH of the human ileum (pH 7.5), in which Eudragit S is commonly used (see column 9, lines 37-41); and 3) Meyer also teaches that the composition is formulated so that the active ingredient is released predominately in the ileum (see abstract), and Amphetamine is a common appetite suppressant drug (see column 1, lines 16-17). Thus, one would be motivated to provide better release profiles of amphetamines by incorporating the specific enteric coating agent disclosed in Applicant's claim 53.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine '011 and a second layer surrounding the first layer and the first layer surrounding the core because Berger teaches that control of the active agent within the body is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings. Thus, it is within the

art to adjust the thickness of the tablet coatings to achieve the desired effects of release in the human body.

(6) Claims 1-4, 6-13, 15-17, 19-26, 28-44, 46-54, 56 and 57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 5-7 of copending Application No. 11/443,151 ('151) in view Berger (US 3,344,029).

This is a provisional obviousness-type double patenting rejection.

The application '151 teaches a pharmaceutical formulation for delivery of a mixture of amphetamine base salts effective to treat ADHD comprising an immediate release dosage form; a delayed enteric release dosage that provides delayed release upon oral administration; and a pharmaceutically acceptable carrier; wherein the composition is sufficient to maintain an effective level of amphetamine base salts in the patient over the course of at least 8 hours without further administration of amphetamine base salt for about a 20 mg total dose, and the peak plasma concentration of amphetamine base salts reached after release of said delayed enteric release dosage form exceeds the peak plasma concentration previously reached after release of said immediate release dosage form (see claim 1). The enteric release dosage form comprises a coating of a thickness of at least 20 μm or 25 μm (see claims 6 and 7) and

the salts are contained in about equal amounts within each of said dosage forms (see claim 5). The formulation further comprises an anionic copolymer and the coating is soluble at a pH of about 5.5 upwards (see claim 6).

The application '151 does not teach the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate. Also, the amphetamine salts coated onto a core or incorporated into a core, or wherein the immediate release and enteric release portions are present on a single core is not taught. Lastly, the properties of the composition and a protective layer are not taught.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the

therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '151 and the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate or wherein the amphetamine salts are provided in about the same

amounts because they are species of the genus amphetamine salts. Without unexpected results, the above amphetamine salts should perform the same as the genus.

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '151 and a protective layer, the amphetamine salts coated onto a core or incorporated into a core, or the immediate release and enteric release portions are present because Berger teaches the following: 1) a tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract; 2) the cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51); 3) a pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24); and 4) further control of dissolution is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6).

The application '151 and Berger compositions are controlled release compositions. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third

composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

(7) Claims 1-5 and 15-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-10, 23, 24, 28 and 31-39 of copending Application No. 11/030,174 ('174) in view of Berger (US 3,344,029).

This is a provisional obviousness-type double patenting rejection.

The application '174 teaches a pharmaceutical formulation comprising a sustained release formulation of at least one amphetamine salt which provides a mean plasma concentration profile in human ADHD patients, wherein at least one amphetamine or amphetamine salt is a mixture of dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate (see claims 6-8, 23, and 31). The amphetamine salts or mixtures thereof is 20 mg (see claim 28). The salts are administered in equal amounts (see claim 8) and are provided in a core, which is coated with a coating comprising a pharmaceutically

acceptable water-insoluble polymer providing sustained release (see claims 9, 33 and 35). The coating further comprises a dissolution regulated agent (i.e. enteric release coating; see claim 10 and 34). The sustained release component is selected from water-soluble polymers, water-insoluble polymers, entero-soluble polymers, and mixtures thereof (see claim 34). The amphetamine component and sustained release component applied form at least one layer around the core (see claim 36), wherein at least one layer comprise a combination of at least one amphetamine component and at least one sustained release component (see claim 37); or wherein each layer is individually comprised of amphetamine components or sustained release components (see claim 38); or wherein alternating layers of amphetamine components and sustained release components are applied to the core (see claim 39).

The application '174 does not specifically teach the properties of the composition, an immediate release coating or the thickness of the enteric release coating of at least 25μ.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46). The cores are coated with alternating coatings of therapeutically active

material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '174 and an immediate release coating and an enteric release coating with a thickness of at least 25μ because Berger teaches that further control of dissolution is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Thus, the thickness of the enteric coated pellet can be adjusted by one skilled in the art to achieve the desired dissolution properties. It is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of the result effective variable in a known process is ordinarily within the skill of the art." See, e.g., In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Paterson* Appeal No. 02-1189 (Fed. Cir. January 8, 2003).

The application '174 and Berger compositions are controlled release compositions. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re*

Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

(8) Claims 1-4 and 15-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 12, 14, 23 and 24 of copending Application No. 11/774,697 ('697) in view of Berger (US 3,344,029).

This is a provisional obviousness-type double patenting rejection.

The application '697 teaches a pharmaceutical formulation for delivery of a mixture of amphetamine base salts (see claim 1) effective to treat ADHD (see claim 16) comprising an immediate release dosage form and a sustained or controlled release dosage form (see claim 23) an immediate release dosage form; wherein a single oral dosage provides amphetamine release in both said earlier and later periods (see claims 1 and 14). The total amphetamine dose per day is about 1 to about 200 mg (see claim 12).

The application '697 does not teach the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate. Neither a specific immediate release coating or

enteric release coating is taught. Also, the amphetamine salts coated onto a core or incorporated into a core, or wherein the immediate release and enteric release portions are present on a single core is not taught. Lastly, the properties of the composition and the thickness of the enteric release coating are not taught.

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of

coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine sulfate and dextroamphetamine sulfate (see column 2, lines 17-18). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '697 and the specific amphetamine salts dextroamphetamine sulfate, dextroamphetamine succharate, amphetamine aspirate monohydrate or amphetamine sulfate or wherein the amphetamine salts are provided in about the same amounts because they are species of the genus amphetamine salts. Without unexpected results, the above amphetamine salts should perform the same as the genus.

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine '697 and a specific immediate release coating or enteric release

coating, the thickness of the enteric release coating, the amphetamine salts coated onto a core or incorporated into a core, or the immediate release and enteric release portions are present because Berger teaches the following: 1) a tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract; 2) the cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51); 3) a pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24); and 4) further control of dissolution is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6).

The application '697 and Berger compositions are controlled release compositions. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d

1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-17 and 19-56 rejected under 35 U.S.C. 103(a) as being unpatentable over Berger (US 3,344,029), in view of Millman (US 2,881,113), in view of Nash et al. (US 2,993,836), in further view of Meyer (US 5,322,697).

Berger teaches a sustained action therapeutic preparation for oral administration in the form of a capsule or tablet containing a plurality of resilient cores each consisting essentially of cohesive intimate admixture of a finely divided therapeutically active material and an ingestible material resistant to disintegration in the gastro-intestinal tract. The variation in the cores between the therapeutic agent and ingestible material provide varying release rates in the gastro-intestinal tract (see column 1, lines 32-35 and 38-46; addresses claims 3, 4, 8, 12, 13 and 22). The cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51; addresses claims 1, 2, 7, 10, 11, 19, 21, 23, 24, 25, 26, 42, 44, 45, 53, 54 and 55). Although the therapeutically active material in the coating is immediately exposed to alimentary canal fluids upon accidental crushing, more than 50% of the therapeutically active material in the cores intimately and cohesively admixed with the ingestible material is not so exposed and is released at a later safe time after being swallowed (see column 1, lines 58-64; addresses claims 1, 10, 15, 19, 42, 43, and 53). The preparation is such that the release of therapeutically active material is more evenly distributed over a given time period (see column 1, lines 67-68). Further control is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings (see column 2, lines 3-6; addresses claims 1, 5, 9, 10, 14, 16, 19, 34, 35 and 53). Therapeutically active materials useful in the dosage units include amphetamines such as dl amphetamine

sulfate and dextroamphetamine sulfate (se column 2, lines 17-18; addresses claims 1, 6, 10, 15, 19 and 53). The ingestible material is at least partially dissolved in methanol (i.e. pharmaceutical carrier; see column 2, lines 54-55; addresses claims 19, 42 and 53). The active material is admixed with sugar and corn starch (i.e. pharmaceutical carrier; see column 3, lines 6-8; addresses claims 19, 42 and 53). A pharmaceutical glaze is coated on top of the cores and coatings (i.e. protective coating; see column 4, lines 4-24; addresses claims 6, 10 and 41). The therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10; addresses claims 33, 36-39, 42, and 52)

Berger does not teach the following: 1) pulsed enteric release (claims 1, 6, 10, and 15); 2) a thickness of at least 25μ or greater than 20μ (claims 1, 9, 16, 34, 35, and 53); 3) the specific amounts of the amphetamine salts (claims 33, 36-39, 42, and 52); 4) a specific delayed release component that is pH independent (claims 40 and 56); 5) properties of the composition, dosage amounts, or method of treatment disclosed in claims 15, 17, 20, 28-30, 36-39, 42, 43, 46-51 and 53; 6) wherein the pharmaceutically active amphetamine salts and immediate release components are provided on one core, and pharmaceutically active amphetamine salts and delayed release components are provided on another core (claim 27); and 7) an anionic copolymer based on methacrylic acid and acrylic acid ethyl ester, and soluble at a pH of about 5.5 upwards (claim 53).

In regards to the method of treatment of the composition, these factors are not considered in composition claims. The claims are only treated on the merits as related to a composition. Also, in regards to the properties of the composition, including the pulsed enteric coating, they are inherent to the composition because where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established. Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). The above applies to claims 1, 6, 10, 15, 17, 20, 28-30, 36-39, 42, 43, 46-51 and 53.

Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22). The amphetamine compounds are added in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3).

Nash et al. teaches an improvement in pharmaceutical sustained release tablets, in which a sustained release tablet breaks down uniformly in an aqueous medium independent of pH and/or the presence of enzymes (see column 1, lines 10-16). Thus, when administered to a patient, the uniform release absorption at a uniform rate

regardless of the part of the gastrointestinal tract in which the tablet lies (see column 1, lines 33-36). Therapeutic agents that are used in the tables are dextro-amphetamine sulfate (see column 2, line 67).

Meyer teaches a composition administered in a tablet form that controls appetite. The composition is formulated so that the active ingredient is release predominately in the ileum (see abstract). The preferred enteric coating is a pH sensitive polymer that dissolves at the neutral to slightly alkaline pH of the human ileum (pH 7.5). A commonly used currently approved coating of this nature is Eudragit S (see column 9, lines 37-41). Amphetamine is a common appetite suppressant drug (see column 1, lines 16-17).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Berger and a thickness of at least 25μ or greater than 20μ because Berger teaches that control of the active agent within the body is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings. Thus, it is within the art to adjust the thickness of the tablet coatings to achieve the desired effects of release in the human body.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Berger and the specific amounts

of the amphetamine salts as disclosed in claims 33, 36-39, 42, and 52 because of the following teachings: 1) Berger teaches that the therapeutically active materials useful in the dosage units are in general those which are normally administered orally and which are administered in relatively exact dosages (see column 2, lines 7-10); 2) Millman teaches a composition consisting of amphetamine compounds, such as dl-amphetamine sulfate and dextroamphetamine sulfate (see column 1, lines 15-22), in equal amounts and from about 3 to about 6 mg of the mixture (see column 2, example 1 and claim 3); and 3) it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Berger and a specific delayed release component that is pH independent as disclosed in claims 40 and 56 because of the following teachings: 1) Berger teaches an amphetamine composition comprising an ingestible material resistant to disintegration in the gastro-intestinal tract (see column 1, lines 32-35); 2) Nash et al. teaches an improvement in pharmaceutical sustained release tablets such as amphetamines, in which a sustained release tablet breaks down uniformly in an aqueous medium independent of pH and/or the presence of enzymes (see column 1, lines 10-16); and 3) Nash et al. also teaches that the composition when administered to a patient, the uniform release absorption at a uniform rate regardless of the part of the gastrointestinal tract in which the tablet lies (see column 1, lines 33-36).

Thus, the benefit to adding a pH independent enteric coating is to provide a uniform release absorption regardless of the part of the gastrointestinal tract in which the tablet lies.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Berger and wherein the pharmaceutically active amphetamine salts and immediate release components are provided on one core, and pharmaceutically active amphetamine salts and delayed release components are provided on another core as disclosed in claim 27 because of the following teachings: 1) Berger teaches that the cores are coated with alternating coatings of therapeutically active material and ingestible material (i.e. enteric coating) and the proportion of therapeutically active material and ingestible material in the cores (see column 1, lines 47-51); and 2) Berger also teaches that control of the active agent within the body is obtained by varying the proportions of therapeutically active material in the cores and in the coatings, varying the number of coatings, and varying the thickness of or number of ingestible material coatings. Thus, to achieve maximum psychological effect, one skilled in the art can layer the composition with the different components above with reasonable levels of expected success.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Berger and an anionic copolymer based on methacrylic acid and acrylic acid ethyl ester, and soluble at a pH of about 5.5 upwards (applicant's claim 53) because of the following teachings: 1) Berger teaches a

composition comprising amphetamines with an enteric coating; 2) Nash et al. teaches an improvement in pharmaceutical sustained release tablets such as amphetamines, in which a sustained release tablet breaks down uniformly in an aqueous medium independent of pH and/or the presence of enzymes (see column 1, lines 10-16); 3) Meyer teaches a tablet that controls appetite comprising a pH sensitive polymer that dissolves at the neutral to slightly alkaline pH of the human ileum (pH 7.5), in which Eudragit S is commonly used (see column 9, lines 37-41); and 4) Meyer also teaches that the composition is formulated so that the active ingredient is released predominately in the ileum (see abstract), and Amphetamine is a common appetite suppressant drug (see column 1, lines 16-17). Thus, one would be motivated to provide better release profiles of amphetamines by incorporating the specific enteric coating agent disclosed in Applicant's claim 53.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KDC

SHEELA PADMANABHAN
SUPERVISORY PATENT EXAMINER